

### **Amendments to the Claims**

This listing of claims will replace all prior versions, and listings, of claims in the application.

#### **Listing of Claims:**

1. – 3. (Canceled)

4. (Currently amended) A polyarginine containing crystal of human growth hormone (hGH), comprising polyarginine and hGH, wherein said hGH is selected from the group consisting of:

- (a) the 191 amino acid sequence of native hGH; and
- (b) the 192 amino acid sequence of said 191 amino acid sequence of native hGH additionally containing an N-terminal methionine.

5. – 6. (Canceled)

7. (Currently amended) A polyarginine containing crystal of human growth hormone (hGH), comprising polyarginine and hGH, wherein said hGH is selected from the group consisting of:

- (a) the 191 amino acid sequence of native hGH; and
- (b) the 192 amino acid sequence of said 191 amino acid sequence of native hGH additionally containing an N-terminal methionine;

wherein the crystal is characterized by a release profile such that a single administration of said crystal to a mammal provides an *in vivo* human growth hormone (hGH) serum concentration profile in said mammal having a T<sup>90%</sup> value higher than that provided by a single

administration of the same amount of soluble human growth hormone.

8. (Currently amended) A polyarginine containing crystal of human growth hormone (hGH), comprising polyarginine and hGH, wherein said hGH is selected from the group consisting of:

- (a) the 191 amino acid sequence of native hGH; and
- (b) the 192 amino acid sequence of said 191 amino acid sequence of native hGH additionally containing an N-terminal methionine;

wherein the crystal is characterized by an insulin growth factor-1 (IGF-1) serum elevation profile such that a single administration of said crystal to a mammal provides an *in vivo* IGF-1 serum elevation over baseline IGF-1 level in said mammal at similar levels compared to those provided by the same amount of soluble human growth hormone (hGH) administered in more than one administration.

9. (Currently amended) A polyarginine containing crystal of human growth hormone (hGH), comprising polyarginine and hGH, wherein said hGH is selected from the group consisting of:

- (a) the 191 amino acid sequence of native hGH; and
- (b) the 192 amino acid sequence of said 191 amino acid sequence of native hGH additionally containing an N-terminal methionine;

wherein the crystal is characterized by a bioavailability such that a single administration of said crystal has a relative bioavailability of at least 50% or more, as compared to that of an identical dose of soluble human growth hormone (hGH) delivered via the same administrative route, wherein said bioavailability is measured by area under curve (AUC) of total *in vivo* hGH serum concentration for said soluble hGH and said hGH crystal.

10. (Original) The crystal according to claim 7 or 8, wherein said mammal is a human.

11. – 16. (Canceled)

17. (Currently amended) A composition comprising the crystal ~~polyarginine-containing crystals~~ according to claim 4, 7, 8 or 9, and an excipient.

18. (Currently amended) The composition according to claim 17, wherein said crystal ~~crystals~~ and said excipient are present in said composition at a molar ratio of hGH:excipient of 1:10 to 1:0.125.

19. (Original) The composition according to claim 17, wherein said excipient is selected from the group consisting of: amino acids, salts, alcohols, carbohydrates, proteins, lipids, surfactants, polymers, polyamino acids and mixtures thereof.

20. (Currently amended) The composition according to claim 17 ~~claim 19~~, wherein said excipient is selected from the group consisting of: protamine, polyvinylalcohol, cyclodextrins, dextrans, calcium gluconate, polyamino acids, polyethylene glycol, dendrimers, polyorthinine, polyethyleneimine, chitosan and mixtures thereof.

21. (Original) The composition according to claim 20, wherein said excipient is selected from the group consisting of: protamine, polyarginine, polyethylene glycol and mixtures thereof.

22. (Previously presented) The composition according to claim 17, wherein the concentration of human growth hormone (hGH) in said composition is between 0.1 and 100 mg/ml.

23. – 59. (Canceled)

60. (Previously presented) The polyarginine containing crystal according to claim 4, 7, 8 or 9, wherein the polyarginine is co-crystallized with the human growth hormone (hGH).

61. (Previously presented) The polyarginine containing crystal according to claim 4, 7, 8 or 9, wherein the polyarginine is complexed with crystals of the human growth hormone (hGH).

62. (Currently amended) The polyarginine containing crystal according to claim 4, 7, 8 or 9, wherein the crystal is produced by co-crystallizing [[a]] the human growth hormone with polyarginine.

63. (Previously presented) The polyarginine containing crystal according to claim 4, 7, 8 or 9, wherein the crystal is produced by:

- (a) crystallizing the human growth hormone, and
- (b) complexing polyarginine to the crystallized human growth hormone.

64. (Currently amended) The polyarginine containing crystal according to claim 4 ~~any one of claims 4, 7, 8, 9, and 60 to 63~~, further comprising a cation.

65. (Currently amended) A pharmaceutical composition comprising the polyarginine containing crystal of human growth hormone of claim 4 ~~claims 4, 7, 8, 9, 62, 63 or 64~~.

66. (New) A pharmaceutical composition comprising the polyarginine containing crystal of human growth hormone of claim 7.

67. (New) A pharmaceutical composition comprising the polyarginine containing crystal of human growth hormone of claim 8.

68. (New) A pharmaceutical composition comprising the polyarginine containing crystal of human growth hormone of claim 9.

69. (New) A pharmaceutical composition comprising the polyarginine containing crystal of human growth hormone of claim 60.

70. (New) A pharmaceutical composition comprising the polyarginine containing crystal of human growth hormone of claim 61.

71. (New) A pharmaceutical composition comprising the polyarginine containing crystal of human growth hormone of claim 62.

72. (New) A pharmaceutical composition comprising the polyarginine containing crystal of human growth hormone of claim 63.

73. (New) A pharmaceutical composition comprising the polyarginine containing crystal of human growth hormone of claim 64.

74. (New) The polyarginine containing crystal according to claim 7, further comprising a cation.

75. (New) The polyarginine containing crystal according to claim 8, further comprising a cation.

76. (New) The polyarginine containing crystal according to claim 9, further comprising a cation.

77. (New) The polyarginine containing crystal according to claim 60, further comprising a cation.

78. (New) The polyarginine containing crystal according to claim 61, further comprising a cation.

79. (New) The polyarginine containing crystal according to claim 62, further comprising a cation.

80. (New) The polyarginine containing crystal according to claim 63, further comprising a cation.